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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/784,537	02/23/2004	Wadih Arap	UTSC:872US	2636

7590 09/22/2006

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/784,537	ARAP ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 48-55* is/are pending in the application.

4a) Of the above claim(s) *10-19 and 53-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2 and 20, 48-52* is/are rejected.

7)☐ Claim(s) *3-9 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/14/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: sequence letter

DETAILED ACTION

Claims 1-21 and 48-55 are pending.

Sequence requirements

This application contains sequence disclosure in line 6 of paragraph 0178, line 1 and 3 in paragraph 0183, line 9 in paragraph 0203 that is encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Full compliance with the sequence rules is required in response to this Office Action. A complete response to this office action should include both compliance with the sequence rules and a response to the Office Action set forth below. Failure to fully comply with **both** these requirements in the time period set forth in this office action will be held non-responsive.

Election/Restrictions

1. Applicant's election of group I in the scope of SEQ ID NO: 1 and conjugating peptide to a drug as a therapeutic agent in the reply filed on July 10,2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-9, 20, 21, 52 that read on the elected scope of SEQ ID NO: 1 and conjugating peptide with a drug are considered. Applicants are reminded to emend claims to the scope for reflecting the examination on the merits.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 48-52 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: how to detect if a peptide that bind to the cell or tissue expressing APA specifically binds to APA rather than other cellular component.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6.

7. Claims 1-2 and 20 are drawn to an isolated peptide and a composition comprising said peptide, which selectively binds to aminopeptidase A and inhibiting aminopeptidase A activity. Regarding claims 48-53, they drawn to a product by process.

8. Regarding to the Product-by-Process Claims, MPEP 2113 [R-1] cites: **PRODUCT-BY-PROCESS CLAIMS ARE NOT LIMITED TO THE MANIPULATIONS OF THE RECITED STEPS, ONLY THE STRUCTURE IMPLIED BY THE STEPS.** "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted) MPEP further cites" The structure implied by the process steps should be considered when assessing the patentability of product-by-process claims over the prior art, especially where the product can only be defined by the process steps by which the product is made, or where the manufacturing process steps would be expected to impart

distinctive structural characteristics to the final product. See, e.g., In re Garnero, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979) (holding "interbonded by interfusion" to limit structure of the claimed composite and noting that terms such as "welded," "intermixed," "ground in place," "press fitted," and "etched" are capable of construction as structural limitations.)

9. In the instant case, claims 48-52 do not define that manufacturing process steps impart any distinctive structural characteristics to the final product compared to the product in the prior art, the patentability of the product cited in claims 48-52 does not depend on its method of production.

10. Claims 1-2, 20 and 48-52 are rejected under 35 U.S.C. 102(b) as being anticipated by Quik et al. (Brain Res. Bull. 1987, Vol. 19, No. 1, pp. 145-147).

11. Quirk et al. teach a peptide that is an aminopeptifase A (AAA) inhibitor, i.e. Amastatin that binds to APA and inhibits the activity of APA (See abstract). Therefore, the claimed invention is anticipated by the cited reference.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 1-2, 20 and 48-52 are rejected under 35 U.S.C. 102() as being anticipated by Georgiadis et al. (Biochemistry, Feb. 2000, Vol. 39, pp. 1152-1155).

14. Georgiadis et al. teach an aminophosphine peptide GluΨ(PO2-CH2)Leu-Ala, which possess the zinc-binding motif, HEXXH found in most zinc-dependent metalloproteinase APA, and exhibits a potent inhibitory activity for aminopeptidase A (APA) by interaction with APA (See abstract and page 1154). Therefore, the claimed invention is anticipated by the cited reference.

15. In this rejection, claims 48-52 are also considered as product-by process. The patentability of the product cited in claims 48-52 does not depend on its method of production.

16. Claims 1-2, 20 and 48-52 are rejected under 35 U.S.C. 102() as being anticipated by David et al. (J. med. Chem, Dec. 1999, Vol. 42, pp. 5197-5211).

17. David et al. teach a method for identifying peptide inhibitor for aminopeptidase A. They have identify several aminopeptidase A inhibitors, wherein one of such peptide of H3N+CH(CH3CH2SO3-)CH9SH)CO-Ile-3-COOH)Pro exhibits potent inhibitory activity against aminopeptidase A at Ki of 0.87 nM (Please see abstract and pages 5198, 5204-5209). Therefore, the claimed invention is anticipated by the cited reference.

18. In this rejection, claims 48-52 are also considered as product-by process. The patentability of the product cited in claims 48-52 does not depend on its method of production.

Claim Rejections - 35 USC § 112

19. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

20. Claims 3 and 5-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for identifying peptide of SEQ ID Nos: 1-3 that are able to bind to APA, wherein peptide of SEQ ID NO: 2 is able to reduce the growth of an exogenous breast cancer implanted in a mouse model and inhibit the neovasculation of blood vessel in Chick embryo chorioallantoic membrane (CAM) assay, does not reasonably provide enablement for having any or all APA binding peptide capable of inhibiting angiogenesis, treating cancer and diabetic retinopathy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

21. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would render undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following: 1). Nature of the invention, 2). Scope of the invention; 3). State of Art; 4). Unpredictability of the field; 5). Number of working examples taught in the specification, 6). Amount of guidance presented in the specification, and 7). Level of skill in the art.

22. In the instant case the nature of the invention is directed to an isolated peptide selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 3, wherein said peptide is able to bind aminopeptidase A, inhibit the aminopeptide A activity, reducing the neovasculation in vivo reduction of the tumor growth. However, the scope of the claims read on any peptide that binds aminopeptidase A that is able to inhibiting angiogenesis and treating cancer and diabetic retinopathy.

23. The state of art teaches that blood vessel development is associated with the malignant tumor metastasis, and the tumor metastasis is associated with the neovasculation of blood vessel around the tumor mass (Fujimura et al. (Oncology 2000, Vol. 58, pp. 342-352). However, treatment of tumor by blocking the blood vessel development or inhibit neovasculation are very complicated processes in vivo, and it is unpredictable whether any aminopeptidase inhibitory peptides is able to inhibit the blood vessel development in vivo.

24. The specification only teaches that peptides of SEQ ID NOS: 1-3 are able to bind to aminopeptidase A and peptide of SEQ ID NO: 2 is able to block the blood vessel formation and inhibit the tumor development. The specification does not produce sufficient evidence to support the broad scope of the claims.

25. Given the above analysis of the factors, which the courts have determined are critical in asserting whether a claimed invention is enabled, it must be considered that the

skilled artisan would have conducted undue and excessive experimentation in order to practice the claimed invention.

Conclusion

Claims 4, 7-8 and 21 are free of rejections. However they are not in condition for allowance because they depend on the rejected claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bao Qun Li
09/13/2006

BAOQUN LI, MD
PATENT EXAMINER

Notice to Comply	Application No.	Applicant(s)	
	Examiner	Art Unit	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☒ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☒ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: See detial in office action

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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